REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 16-44 will be pending in the application subsequent to entry of this Amendment.

Certified Copy of Italian Priority Document

As a preliminary matter, a WIPO-certified copy of the priority document IT RM2002A000194 filed April 9, 2002 is being submitted separately with this paper.

Claim Interpretation if Faulty

In item 1 of the Official Action relating to the specification, the examiner indicates that "claims 1-15 are interpreted as being drawn to methods of preparation". In fact, this is incorrect. These claims are cast in the typical European "method of use/method of treatment" style. The new claims presented above are cast in traditional U.S. method of treatment style and have been prepared responsive to the examiner's comments in items 5-9 of the Official Action.

Amendments to the Specification/Abstract

Pages 3-6 include a discussion of arrangement of the specification. This application is a national phase entry of a PCT application and thus is compliant with PCT requirements which, in turn, are accepted in national filings in the United States. For convenience, selected topical headings have been included and those not included are simply not relevant to the description of the invention. A substitute specification is provided showing the changes and appropriately marked.

The Abstract has been amended to conform to the amended claims.

The examiner will note that applicants are seeking correction of the spelling of the family name of the first listed inventor which is listed as Giorgio Cavillini – it should be Giorgio Cavallini.

Response to Claim Rejections – 35 USC §102

Regarding the rejection in **item 10**, claims 1-9, examined as directed to methods of preparation, were rejected as being anticipated by Fassi US 6,255,346. Fassi US discloses:

a composition comprising L-carnitine (LC), acetyl L-carnitine (ALC) and propionyl L-carnitine (PLC) or the pharmacologically acceptable salts thereof;

a method of suppressing withdrawal symptoms and the craving for alcohol comprising administering to an individual an effective amount of a combination of L-carnitine, acetyl L-carnitine and propionyl L-carnitine or the pharmacologically acceptable salts thereof; and

a method of preventing the abuse of alcohol in substantially healthy individuals, said method comprising administering to an individual an effective amount of a combination of L-carnitine, acetyl L-carnitine and propionyl L-carnitine or the pharmacologically acceptable salts thereof. (abstract and claims).

Applicants' new claims 16-44 directed to the treatment of oligoasthenoteratospermia are novel over the disclosures of Fassi US.

Regarding **item 11**, claims 1-10, examined as directed to methods of preparation, were rejected as being anticipated by Fassi WO03/066573. Fassi WO discloses (pages 13 and 14):

A dietary kit which comprises:

a) at least one first container containing a dose of L-carnitine zinc citrate and a dose of a further pharmacologically acceptable salt of L-carnitine; and

b) at least one second container containing a dose of arginine.

or comprises:

a1) at least one first container containing acetyl L-carnitine zinc citrate and a further pharmacologically acceptable salt of acetyl L-carnitine; and

b1) at least one second container containing arginine where in a) or a1) can also contain a pharmacologically acceptable salt of propionyl L carnitine (PLC), the molar ratio LC/ALC/PLC ranging from 4:1:0.5 to 1:4:2.

The kit is suitable for counteracting sexual disorders in male subjects, (sperm mobility and concentration in seminal fluid of sub-fertile males) and for treating idiopathic asthenospermia), *see* page 1.

Present claims 16-31 refer to a method for the treatment of oligoasthenospermia comprising administering to a patient in need thereof an effective amount of a combination of L-carnitine, acetyl L-carnitine and propionyl L-carnitine inner salts, or of their pharmaceutically acceptable salts. These salts do not include zinc citrate.

Neither Fassi US6,255,346 nor Fassi WO03/066573 anticipate the content of claims 16-44. New claims 16-44 directed to the treatment of oligoasthenoteratospermia are novel over the Fassi US and WO citations.

Response to Claim Rejections – 35 USC § 103

Regarding the rejection in **item 12**, claims 1-10, examined as directed to methods of preparation, were rejected as being obvious over Cavazza EP 053 933. Cavazza EP discloses the use of L-carnitine (LC) and 2-6-acyl carnitine for the treatment of idiopathic oligoasthenozoospermia [reduced concentration and motility] (col.1, lines 1-4). Cavazza EP 053 933 mentions that 2-6 acyl carnitines are those listed in col. 1, lines 9-10, wherein propionyl L-carnitine is included.

Cavazza's method provides for the administration of only one type of carnitine which can be LC or a 2-6 acyl carnitine.

The clinical study disclosed from col. 1, line 55 to col 2, line 10 enables only the administration of LC, since no clear indication is give as to possible useful effect of the other acyl carnitines. Cavazza EP 053 933 does not give any suggestion on which acyl carnitine can be selected as a good alternative to LC.

Thus, the teaching of Cavazza EP 053 933 is a method for improving the concentration and mobility of spermatozoids [treatment of oligoasthenospermia] which results from the administration of L-carnitine.

Cavazza WO99/27925 discloses an admixture of L-carnitine and acetyl L-carnitine effective in improving sperm concentration and motility and methods for treating humans suffering from idiopathic asthenozoospermia [reduced motility] (page 4, 1st-3rdpar.; page 5, 6th par.). The clinical study reported in Cavazza WO99/27925 show that the combination between LC and acetyl LC gave better results in improving sperm motility in comparison with the single active agents alone.

Cavazza WO99/27925 suggests that the combination of LC and ALC is effective in

improving motility of spermatozoids [treatment of asthenozoospermia].

Thus, Cavazza WO99/27925, 8 years later than Cavazza EP053933, made a selection within the acyl carnitine choices, suggesting that acetyl carnitine is effective in treating asthenozoospermia. Cavazza WO99/27925 does not point to or suggest propionyl LC as a particularly efficacious agent in treating asthenozoospermia.

On the other hand, the present application provides and claims a method for the treatment of oligoasthenospermia by administering to a patient in need thereof an effective amount of a combination of L-carnitine, acetyl L-carnitine and propionyl L-carnitine, as discussed above.

The specification states, on page 48, 2nd par., that the combination of LC and ACL was used as a reference compound during the study on the activity of the claimed combination LC/ALC/PLC. Moreover, it is underlined (page 9, 4th par.) that the claimed combination increases sperm concentration and mobility, and percentage of spermatozoa with a rapid linear progression more efficiently than the combination between L-carnitine and acetyl L-carnitine.

Thus, the present application gives an improvement in respect to the prior art . This improvement could not be predicted by looking at Cavazza WO99/27925 in view of Cavazza EP 053 933 for the following reason:

Cavazza EP 053 933 does not unambiguously suggest that propionyl LC is active in oligoasthenozoospermia, since the examples refers to LC only and no data at all are reported on the activity of each of the other acyl carnitines.

The person skilled in the art could not know that, by adding propionyl LC to the combination of Cavazza WO99/27925, he would succeed in improving the treatment of oligoasthenozoospermia, because he had not at his disposal any pointer from the prior art that motivates him to select propionyl LC among the other acyl carnitines.

Therefore, the combination of Cavazza WO99/27925 and Cavazza EP 053 933 does not render obvious newly amended claims 16-44 and applicants respectfully request the obviousness objection be withdrawn.

For the above reasons it is respectfully submitted that the new claims presented above directed to the treatment of oligoasthenoteratospermia define inventive subject matter. Reconsideration and allowance are solicited.

Respectfully submitted,

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